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1. Your reference

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9827164.6

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3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Millipore Corporation
80 Ashby Road
Bedford
Massachusetts 01730, U.S.A.

Patents ADP number *(if you know it)*

6.5C 91021

If the applicant is a corporate body, give the country/state of its incorporation

A Corporation of Masssachusetts

4. Title of the invention

CHROMATOGRAPHY COLUMN SYSTEM AND METHOD OF PACKING A CHROMATOGRAPHY SYSTEM

5. Name of your agent *(if you have one)*

Graham Watt & Co
Riverhead
Sevenoaks
Kent TN13 2BN

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

Patents ADP number *(if you know it)*

1685001

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

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Signature [signature] Date

GRAHAM WATT & CO 9th December 1998

12. Name and daytime telephone number of person to contact in the United Kingdom

A.D. Wadeson
01732 450055

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CHROMATOGRAPHY COLUMN SYSTEM AND METHOD OF PACKING A CHROMATOGRAPHY SYSTEM

The present invention relates to chromatography columns and in particular to a chromatography column system and method of packing a chromatography column.

Frequently it is desirable to separate out one or more useful components from a fluid mixture that contains other components which may not be useful or are less valuable. To accomplish this it is often necessary or desirable to fractionate such a fluid mixture to separate out the useful or desired components. This can be carried out by using liquid chromatography systems. Liquid chromatography may briefly be described as the fractionation of components of a mixture based on differences in the physical or chemical characteristics of the components. The various liquid chromatographic systems fractionate the components with a fractionation matrix. Some liquid chromatographic matrix systems fractionate the components of a mixture based upon such physical parameters as molecular weight. Still other liquid chromatographic systems will fractionate the components of a mixture based upon such chemical criteria as ionic charge, hydrophobicity, and the presence of certain chemical moieties such as antigenic determinants or lectin-binding sites on the components.

Chromatography systems of various sized are used in

both laboratory analysis operations and for industrial scale production operations in which separation steps such as separating out a fraction from human blood or separating out impurities from a pharmaceutical can be carried out on a large scale in a batch process.

The development of chromatography columns has aimed at providing ease of operation and various additional benefits which have particular commercial importance. These include: (a) the ability to be sterilized by autoclaving; (b) improved sanitation by virtue of design features giving less carryover of product from one batch to the next; (c) the ability to resist solvents; (d) material conformity to food grade FDA regulations; (e) an improved pressure tolerance; (f) lower cost; and (g) the potential for full or partial automation.

Traditionally, a chromatography column must be disassembled to reslurry and remove chromatography media in order to repack the chromatography column with fresh chromatography media or with different chromatography media specific for an application. This procedure has several problems. First, the time required to perform this operation is substantial, especially with large industrial columns, and results in lost productivity in a commercial operation. Second, the constant assembly and disassembly of the chromatography column creates excessive wear on the

components and leads to a reduced life of the chromatography system. Third, mechanical lifting equipment and significant floor and head space are required. finally, each time a chromatography column is disassembled there are increased opportunities for unwanted contaminants to be introduced into the column, which can subsequently contaminate the fluid mixture and fraction of interest.

Another problem associated with some types of chromatography columns is the inability to clean the flow path used to introduce chromatography media into the chromatography column while maintaining a barrier between the cleaning solution and the packed chromatography media.

A known chromatography column is illustrated in Figure 1, which employs two valves, one is located at the top of the column and the other spaced from it at the bottom. Each valve has three ports. Port 1 is for feeding slurry into the column during packing and for pumping liquid into the column for reslurrying during unpacking. Port 2 is for expelling "clean" liquid pumped via port 1 to flush out the slurry line after packing, and for removal of reslurried gel during unpacking. Port 3 is the inlet and outlet for the mobile phase, and communicates directly with and only with the distribution cell.

The valves 11 are each as shown in more detail in Figure 2 in which a pneumatically actuated valve sleeve can

assume three different positions depending upon the mode of operation. In the bottom valve during packing, the valve sleeve is in the semi-retracted packing position, as shown in Figure 2, which closes off port 2 from communication with the inside of the column. When in this position, slurry is pumped into the column via port 1 of the bottom valve, and air or excess liquid is removed via port 2 of the top valve. When the column is purged of air, the valve sleeve of the top valve is in the closed position (i.e. fully extended into the housing).

In the run position, the valve sleeves for both the top and bottom valves 11 are in the unactuated position, closing port 1 and port 2 of both valves from the inside of the column. When in this position, clean liquid can be pumped from port 1 to port 2 to remove any media (gel) left in the slurry line or to carry out a clean-in-place ("CIP)" cycle on these lines. The column is then run by pumping mobile phase through port 3 to (and from) the distribution cell.

There are three methods to reslurry a packed bed employing these valves. In the first method, the bottom valve is in the fill (valve sleeve partly retracted) position and the top valve is in the drain position where the valve sleeve of the top valve is fully retracted from the column housing. When the valve sleeve of the top valve

is in this position, clean liquid can be pumped via port 1 through the nozzles at the end of the tube to reslurry the gel, which is then removed through port 2. In the second method, both the bottom and to valves are in the drain position (with the sleeves fully retracted). Clean liquid is pumped into the column via port 1 of either the top or bottom valve to reslurry the gel. Reslurried material passes out through the bottom of the column. In the third method, the top valve is in the fill (sleeve partly retracted) position and the bottom valve is in the drain (sleeve fully retracted) position. This enables slurrying of the top of a packed bed and the slurry passes out of the bottom valve. All three methods can be used in combination during a reslurry operation.

To drain or empty the column, both top and bottom valves are in the drain position and either pump is reversed to withdraw liquid from the column. Alternatively, a combination of pumps may be used to inject and drain the column simultaneously through port 2 on either valve. In addition, slurry may be recycled to the column to greatly reduce the quantity of clean liquid needed to flush the column.

The above described prior art valve has a rather complex construction to ensure the sleeve adopts the required operative positions with implications for

reliability and manufacturing costs.

The chromatography column of PCT/GB97/02943 discloses a chromatography column which can provide the same functional capabilities of the above described prior art column, with a valve of reduced complexity, and so more economic to manufacture which can provide increased reliability and be operable to vent the volume in the event of accidental over-pressurization. This column is shown in Figures 3 and 4.

The valve has two operative positions, only, thereby allowing a reduction in the complexity of the valve. Because the central bore and passageway are always in fluid communication, should there be an accidental over-pressurization of the column during packing via the passageway in the longitudinal member, the media can enter the central bore thereby venting the column and relieving the overpressure. This is in contrast to the situation in which an over-pressurization occurs during packing with the above described prior art valve as the passageway and central bore are not in fluid communication during packing so no venting is possible if only one valve is present.

A known method of packing such columns is to prepare a slurry in which one or more solutes are transferred from a fluid to the surface of a solid phase where they are adsorbed include contacting of the component with the solid

particles by the passage of flow through a packed chromatography bed and batch adsorption of the component or a product of a in-situ reaction onto the solid particles in a stirred tank and then gravity settling or other traditional column packing techniques to form a packed bed.

The present invention seeks to provide an improved chromatography column system and method of packing a chromatography column, which system and method are as claimed in the claims.

A method according to a first aspect of the present invention is a method of packing a chromatography column with a chromatography media from a slurry vessel in which a slurry containing the chromatography media is pumped into the chromatography column to pack the column and excess fluid from the chromatography column during packing is returned to the slurry vessel.

The media can be added to the vessel bit by bit until the column is fully packed so reducing the waste that can be associated with prior art packing methods where the initial quantity of media should be at least what is required for packing to ensure the vessel does not become exhausted of media before packing is completed.

A method according to a second aspect of the present invention comprises preparing a slurry including a chromatography media prior to packing a chromatographic

column with the chromatography media including adding th components of the slurry to a slurry vessel and then circulating the slurry from the slurry vessel and returning them to the slurry vessel.

The chromatography media and the liquid components including a target component are introduced into the vessel and the mixture circulated from and back to the vessel to prepare the slurry. This provides a self contained batch adsorption operation where the chromatography media is contacted by components in the fluid and adsorption occurs. The slurry is then pumped in the chromatography column to effect packing of the column. Subsequent recovery of these components can then be effected by a chosen chromatographic procedure.

BRIEF DESCRIPTION OF THE DRAWINGS

In order that the present invention may more readily be understood the following description is given, merely by way of example, with reference to the accompanying drawings, in which:

Fig. 1 is a cross section of a prior art chromatography column including a slurry valve;

Fig. 2 is a longitudinal cross section of the prior art slurry valve of Fig. 1;

Fig. 3 is a longitudinal cross section of the chromatography column of PCT/GB97/02943 with the slurry

valve in the running position;

Fig. 4 is a longitudinal cross section of the chromatography column of Figure 3 with the slurry valve in the unpacking/packing position; and

Fig. 5 is a schematic drawing of the chromatography system of the present invention and with which the method of the present invention can be performed.

DETAILED DESCRIPTION OF THE INVENTION

Referring now to the drawings, Fig. 3 shows the chromatography column fitted with two slurry valves constructed in accordance with the principles of the present invention. In the embodiment shown, the column is comprised of an upper adjustable cell assembly, a hollow cylindrical housing preferably constructed of stainless steel, and a lower fixed cell assembly. Both cell assemblies have slurry valves positioned at the centre. The present invention includes within its scope embodiments wherein the adjustable cell assembly is at the bottom of the column, and the fixed cell assembly is at the top.

The details of the central slurry inlet/outlet valves 11 may be understood with reference to Figs. 3 and 4. The valves comprise a housing having a central bore 15 communicating with three ports. A fixed longitudinal member 18 is located in central bore 15 and itself has a central lumen which serves as a slurry feed line 30. The

slurry feed line 30 communicates at one end with port 1 and at its opposite end with the interior of the column through radially disposed passageways 20. The longitudinal member terminates in a domed head 17 that extends into the column at all times. The longitudinal member 18 has an annular portion 19 reduced in diameter to accommodate, in a sealing manner, the valve sleeve 7 as will be discussed in greater detail below.

The three ports of each of the valves 11 are used as follows: port 1 for pumping slurry through a slurry feed line 30 into the column, and for pumping liquid into the column for reslurrying during unpacking; port 2 for removal of reslurried gel during unpacking; and port 3 which is the inlet and outlet for the mobile phase, this port communicating directly with, and only with, the distribution cell 6.

Ports 1 and 2 may be closed off from the column by means of an annular valve sleeve 7 slidably positioned in the central bore 15. The valve sleeve 7 includes an upper portion 7a, which is L-shaped in cross-section. The upper portion 7a includes a pin hole 4 for receiving pin 4' in order to lock the valve sleeve 7 in its raised position as shown in Figure 4. The valve sleeve 7 also includes an annular lower portion 7b. The bottom end of the lower portion 7b includes an annular lip 24 adapted to seal

against the head 17 in the running position (Fig. 3). The annular lip 24 and longitudinal member 18 are dimensioned such that as the seal between lip 24 and longitudinal member 18 is broken a gap is created with the annular reduced diameter portion 19 of the longitudinal member, so as to provide fluid communication between the central bore 15 and the passageway 9 to the column interior simultaneously as the seal between the sleeve 7 and annular lip 24 is broken. The valve sleeve 7 may be actuated by any suitable means, such as manually, or electrically, or hydraulically, or preferably pneumatically.

In this prior art valve the sleeve 7 is driven axially by application of compressed air through either of two pneumatic ports 22 and 23.

In particular, the sleeve 7 has an outwardly extending land 24′ slidable within a cylindrical wall portion 25 of the valve body, and an inwardly extending land 26 and an outwardly extending land 27 at the same axial positions just above the port 2, such that the outwardly extending land 27 slides along the same cylindrical surface 25 of the valve body and the inwardly extending land 26 slides along a cylindrical exterior of an upper part of the fixed body 18 of the valve.

Below the land 24′ of the sleeve 7, the valve housing has an inwardly extending land 31 which will be fixed in

position and which, together with the land 24 on the moving valve sleeve 7, defines a fluid pressure chamber portion 28 of the central bore, isolated from another chamber portion 29 into which the third port 3 opens and which communicates with the distribution cell 6.

The inner pneumatic port 22 thus provides a means of applying pressure to the sealed space 28 below the land 24 for the purposes of retracting the sleeve 7 (moving it relatively upwardly from the Figure 3 position). Similarly application of compressed air to the outer pneumatic port 23 applies pressure above the twin lands 26 and 27 and drives the sleeve 7 axially inwardly (downwardly from the Figure 4 position). In this manner the axial movement of the sleeve can be effected.

However, this pneumatically activated axial movement of the sleeve 7 is required to cause it to occupy one of two different positions and these positions are defined by virtue of the pin 4' which co-operate with the hole 4 of the valve sleeve 7.

Figure 4 shows the "packing" position in which slurry can be discharged from the head 17 of the fixed longitudinal member 18 by virtue of retraction of the sleeve 7 upwardly to the Figure 4 position) so that it exposes the nozzles 20 of the head 17. In this position the pin 4' must be retracted. By positively checking that

the pin 4′ driven by the actuator 8 extended again into hole 4 there is achieved a feedback which confirms that the sleeve is in the "packing" position. This positioning of the pin 4′ in the actuators 8 is checked by virtue of reed switch 8′ of the actuator.

When the valve sleeve 7 is to be extended to the "running" position for the purposes of leaving valve port 3, only, open to the media in the bed by way of the filter mesh of the distribution cell 6, the pin 4′ must be retracted in order to allow the sleeve 7 to pass downwardly to the Figure 3 position. The pin 4′ is then driven by the actuator 8 to extend above the upper rim of the valve sleeve 7 to hold it firmly in the "Running" (Figure 3) position. Positive feedback checking of the position of the valve is derived by checking that pin 4′ is extended, again using the reed switch 8′.

When finally the valve sleeve 7 is to be fully retracted, again, to the "unpacking" position shown in Figure 4 it reaches a fully raised position as viewed in Figure 4 and pin 4′ can now engage in its hole 4 so that the positive feedback checking action by the reed switches 8′ checks that the pin 4′ is advanced.

If the pneumatic control system energising the actuator 8 fails to detect that the pin 4′ is advanced when the "unpacking/packing" position of Figure 4 has been

selected then there will be a malfunction indicated to show that the valve is not fully open. Likewise, if in the Figure 3 position the pin 4′ is not confirmed as being fully extended then again a malfunction will be indicated to show that the sleeve has not descended to the "running" position of Figure 3.

The valve is thus positively driven upwardly and downwardly and the location of it is each of its two positions is clearly defined by the pin 4′ driven by the actuator 8 and checked by the reed switch 8′ of this actuator.

Additionally the valve member may be biased axially (in this case downwardly as viewed in Figure 4) by an optional helical compression spring 9 around the fixed longitudinal member 18 and pressing downwardly against the inwardly directed land 26 of the valve sleeve. Thus the default position, when the air supply 10 is disconnected from the pneumatic control circuit after packing or for storage, is the "Running" Fig. 3 position, closing ports 1 and 2 off from the column. This occurs when the air pressure at pneumatic port 23, and optionally the force of spring 9, forces the valve sleeve 7 to the closed position (Fig. 3). As indicated above the valve sleeve 7 is held in closed position both by the axial forces and the locking pin 4′ of the pneumatic actuator 8 being extended above the

top of the sleeve. This prevents the sleeve 7 from opening inadvertently or due to operating pressure in the column. Those skilled in the art will understand that the description of a pneumatically actuated valve sleeve is for illustrative purposes only; the claims set forth below are intended to encompass any means for actuating the valve operation, including both automated, electrical pneumatic valve opening and/or closing, as well as manually actuated adjustments to the positioning of the valve sleeve 7.

The pneumatic control circuit to operate the actuator 8 will be readily apparent to the man skilled in the art and is not described herein in detail.

One typical operation of the inlet/outlet slurry valves 11 is as follows. Starting from the unpacking position shown in Figure 4, the lower slurry valve 11 remains in the same position as shown in Figure 4. Port 2 is isolated external to the device possibly by means of any known pressure relief device V. In this position both port 1 and 2 communicate with the internals of the column 6.

The inclusion of a pressure relief device in-line with port 2 during the packing operation provides a means for venting the column 6 in the event of incorrect operation.

The upper slurry valve 11 must then be placed in the "running" (Figure 3 position) which requires the actuator 8 to withdraw the pin 4′ from the hole 4, allowing the

pneumatic pressure on the outer pneumatic port 23 to drive the sleeve still further forwardly until the Figure 3 position is attained. At this point the actuator 8 is then operated to advance the pin 4' so it sits just above the axially outer rim of the valve sleeve 7 and holds the sleeve against retraction from the Figure 3 position.

In this position, the annular lip 24 seals against the head 17, thus closing ports 1 and 2 from the column 6. Slurry is fed, for example by a pump, through port 1 of the bottom slurry valve 11 and the slurry feed line 30 into the column. The chromatography media is retained in the column by the distribution cell 6 of the adjustable cell assembly 13, while air and the liquid forming the slurry with the chromatography media are removed, initially venting through port 2 of the top valve 11 until the column is purged of air, and subsequently through port 3 of the upper slurry valve 11.

When the packing of the column with chromatography media 14 is complete, the pneumatic control circuit places the valve sleeve 7 of the lower slurry valve 11 into the closed/running position (Fig. 3) in the manner just described for the upper valve 11, thus closing off ports 1 and 2 from the column. This creates a flow path through slurry feed line 30 and central bore 15 from port 1 to port 2, through with a cleaning solution can be fed, for example

by a pump, to clean in place port 1, pot 2, and the slurry feed line 30. This cleaning operation can be performed at the same time as the processing of the liquid to be separated to prevent the settling and hardening of any residual chromatography media 14 in the slurry feed line 30. This operation of cleaning can be made to automatically follow setting the slurry valve to closed/running for operator convenience.

The chromatography column is now ready to separate the mixture of interest. The mixture (mobile phase) to be separated is fed, for example by a pump (not shown), through port 3 of either the upper or bottom slurry valve 11 into the column through the distribution cell 6 and then flows through the chromatography media 14 and is removed through port 3 of the other slurry valve 11.

After the mixture of interest has been separated, or if for any other reason, it becomes necessary or desirable to reslurry and remove the chromatography media 14, the upper slurry valve 11 and the bottom slurry valve 11 are placed in the unpacking position (Fig. 4), where pin 4' is engaged in pin holes 4. This causes the bottom portion 7b of the valve sleeve to be fully retracted, allowing communication between the column interior and the central bore 15. This unpacking position is achieved from the running position by firstly operating the actuator 8 to

retract the pin 4' from the hole 4, and then applying pressure to the inner pneumatic port 22 to retract the valve sleeve 7 (and in so doing overcome the spring force of the optional spring 9) until the end position of travel is reached where the sleeve 7 is fully retracted. At this point the actuator 21 can operate to advance pin 4' into the hole 4 of the sleeve. Only when this pin has been advanced is there attainment of the positive feedback signal from the reed switch 8'.

Clean liquid is initially introduced into the column (such as by a pump) via port 1 of the bottom slurry valve 11, which reslurries the chromatography media 14 which is removed through port 2 of the bottom slurry valve. Removal of chromatography media slurry by port 2 may be assisted by a second pump (not shown) in which case the upper slurry valve 11 is placed in the unpacking position. The clean liquid is then switched to be introduced via port 1 of the top valve. The effect is to wash out a core of packed chromatography media from near the top valve and from near the bottom valve. An additional but optional method of unpacking is the backflush through the filter mesh of the lower distribution cell 6 to fluidize the media (gel) to assist draining of slurry from the column.

After a short period the dilute slurry washed from the column can be recycled to the port 1 of the top valve in

place of clean liquid, thereby reducing the quantity of clean liquid required.

Clean liquid or a sanitizing agent may be used for the final flushing of the column. The use of a slurry valve 11 on both the upper and bottom cell assemblies facilitates the loading and removal of chromatography media 14 through either the top or bottom of the column. Another benefit of using a slurry valve 11 on both the upper and bottom cell assemblies is the ability to flow the mixture to be separated in either a top-to-bottom, or bottom-to-top flow path. By judicial use of slurry or fresh buffer, it is possible to minimize the volume of liquid needed to re-slurry the contents of the column and empty the column of gel. It is understood that the use of two valves in the preferred embodiment is meant for the purposes of illustrating many of the versatile uses of the valve, and is not meant as a limitation. Those skilled in the art will realize that it is possible to use only one slurry valve, on either the upper or bottom cell assembly, although the performance options would be more limiting. All such modifications which do not depart from the spirit of the invention are intended to be included within the scope of the appended claims.

Particular regard has been made to the cleanability of the valve. Sanitary design has been applied to the type of

hose couplings, material selection and finish, sealing technology and method fro cleaning in place (CIP). The valve may be cleaned in place when in the running position (Figure 3), leaving no unswept surfaces. The profile, location, number and material used for the seals 21 is particularly important. Suitable materials include EPDM, PTFE or composite materials for the seal material.

Once the internal passages through ports 2 and 1 have been cleaned in place, the valve can either be blown through with air or left full with fluid, and all connections for pneumatic actuation and slurry process lines can be disconnected. This enables the column to either be stored or operated in the running Figure 3 position, without attachment to a station for transferring slurry to or from the column.

The pneumatic control circuit provides positive locking positions for each of the three positions of the valve sleeve 7 and positive feedback confirmation of those positions. By use of positional indicators on the pneumatic control circuit, it is possible to provide affirmative feedback of the sleeve position to provide operator validation information. One indicator is used for this in the preferred embodiment, but more can be used as will be readily appreciated by those skilled in the art.

Referring now to Figure 5, a chromatography column

system 100 includes a chromatography column 101 as previously described with reference to Figures 1, 3 and 4 and including top and bottom a valve as shown in Figures 3 and 4 of which ports 1 and 2 are referenced.

A slurry vessel 102 is partially filled with a slurry 104. An output pipe 106 from the bottom of the slurry vessel 102 leads to a T-junction 108 and hence as an input to a packing pump 110 and to a 3-port valve 112 via pipe 113.

The output of the packing pump 110 is coupled to a 3-port valve 114 by a pipe 116 and from there to the base of the chromatography column 101 by a pipe 118. The 3-port valve 112 is also coupled to a pipe 120 which joins the pipe 118 as so also leads to the bottom of the chromatography column 101 and by a pipe 122 to a circulating pump 124 whose output is coupled to a pipe 126 and hence to the slurry vessel 102 via a pipe 128.

Upper port 1 of the chromatography column 101 is coupled to pipe 128 by a pipe 130. Upper port 2 of the chromatography column 101 is coupled to the 3-way valve 114 by a pipe 132.

The chromatography system 100 operates as follows. As a first, optional phase, the suspension 104 containing a fluid mixture including a target molecule and the chromatography media are introduced into the slurry vessel

102. Valve 112 is operated to interconnect pipes 113 and 122 and pump 124 started thereby circulating the media from and back to the slurry vessel via pipes 106, 113, 122, 126 and 128 to prepare the slurry 104.

After sufficient adsorption has taken place of the target molecule and chromatography media the resultant slurry is ready for passing through the chromatography column 101 for packing the column 101 to pack the column with the chromatography media.

Valve 112 is now closed and valve 114 opened so as to couple pipes 116 and 118. On now operating pump 110 the slurry is pumped to the base of the chromatography column 101 via lower port 1.

In the known method of packing such a column the slurry 104 fills the column 101 and when the column 110 is full of slurry 104, excess fluid exhausts through the upper bed support and process port 3 (of Figures 3 and 4) of the upper valve assembly and the particles with the adsorbed molecule are retained against the top bed support. As this process proceeds the packed bed forms against the top sinter and packing is complete when the exhaust flowrate has reduced to zero i.e. when the pressure within the column is equivalent to the pressure set on the pumps. This exhaust fluid is transported to a liquid vessel for disposal, or for use during the unpacking process. It is

to be noted the slurry concentration is maintained constant throughout the packing procedure. The method of the present invention, which ensures that all media particles with the adsorbed molecule are packed within the column, is as follows.

Upper port 1 is opened during packing so the excess fluid is returned to the slurry vessel 102 via pipes 130 and 128 rather than being taken to a waste vessel for other storage vessel. This acts to dilute the media particles in the slurry 104 as packing progresses until all the particles have been retained within the column.

Chromatography media can be gradually added to the vessel until the column is packed thereby minimising the amount of media used to obtain a packed column. The return of the excess fluid to the vessel 102 also assists in the prevention of sedimentation of the slurry during the packing procedure.

Some of the advantages of embodiments of the system and method of the present invention can be summarised as follows:

a) Batch contact between the chromatography media and the target molecule is achieved by the use of the fluid recycle loop, providing continuous agitation in a low shear environment and without the use of mechanical electrically driven

equipment.

b) Full containment during the contact stage and the packing phase of the process.

c) The system and method are based on existing technology and can generate a packed bed within the column by a method which has the benefits of containment and the elimination of manual handling of column component parts.

d) Reduction in the time required to form an efficient packed bed, which can be important as biological materials are susceptible to conformational changes or loss of bioactivity with time. Any reduction in process time assists in the prevention of any loss of product activity.

CLAIMS

1. A method of packing a chromatography column with a chromatography media from a slurry vessel in which a slurry containing the chromatography media is pumped into the chromatography column to pack the column and excess fluid from the chromatography column during packing is returned to the slurry vessel.

2. A method as claimed in claim 1 further including circulating the slurry from the slurry vessel and back to the slurry vessel, either continuously during the packing of the chromatography column or while the packing of the chromatography column is temporarily suspended.

3. A method of preparing a slurry including a chromatography media prior to packing a chromatographic column with the chromatography media including adding the components of the slurry to a slurry vessel and then circulating the slurry from the slurry vessel and returning them to the slurry vessel.

4. A method of packing a chromatography column with a chromatography media comprising preparing a slurry containing the chromatography media prior to packing of the chromatography column as claimed in claim 3 followed by packing the chromatography column with the chromatography media by the method of claim 1 or 2.

5. A chromatography column system including a

chromatography column and a slurry vessel, a pump means for pumping a slurry containing chromatography media from the slurry vessel to the chromatography column to effect packing of the chromatography column and a transport means arranged to transport excess fluid output from the chromatography column during packing back to the slurry vessel.

6. A chromatography column system as claimed in claim 5 including a further pump means operable to circulate the slurry from the slurry vessel and back to the slurry vessel without passing through the chromatography column.

ABSTRACT (ref. Fig. 5)

CHROMATOGRAPHY COLUMN SYSTEM AND METHOD

OF PACKING A CHROMATOGRAPHY COLUMN

A method of packing a chromatography column (101) with a chromatography media (104) from a vessel (102) in which the chromatography media (104) is pumped into the chromatography column (101) to pack the column and excess fluid from the chromatography column during packing is returned to the vessel (102) to dilute the chromatography media.

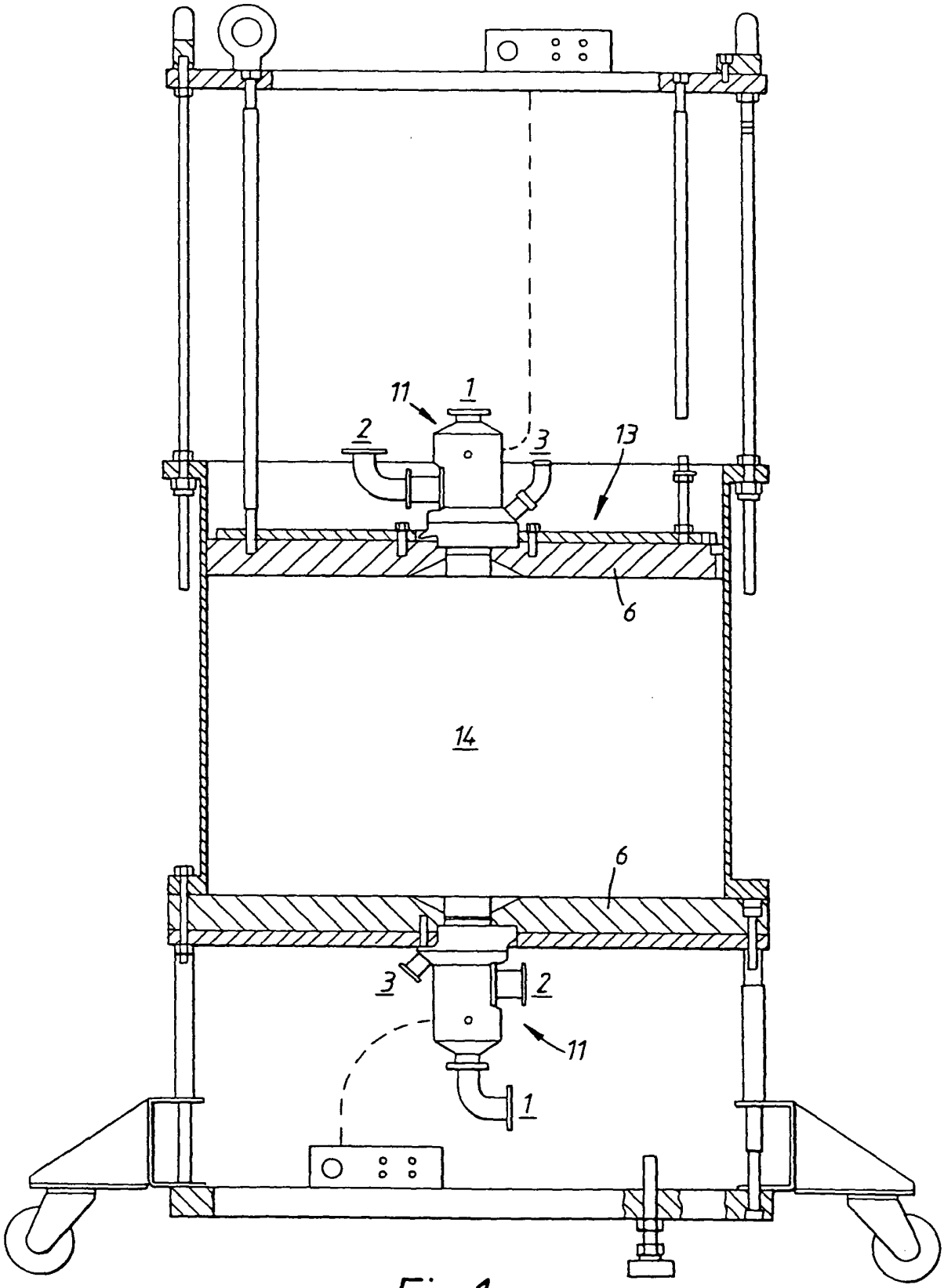

Fig. 1 (PRIOR ART)

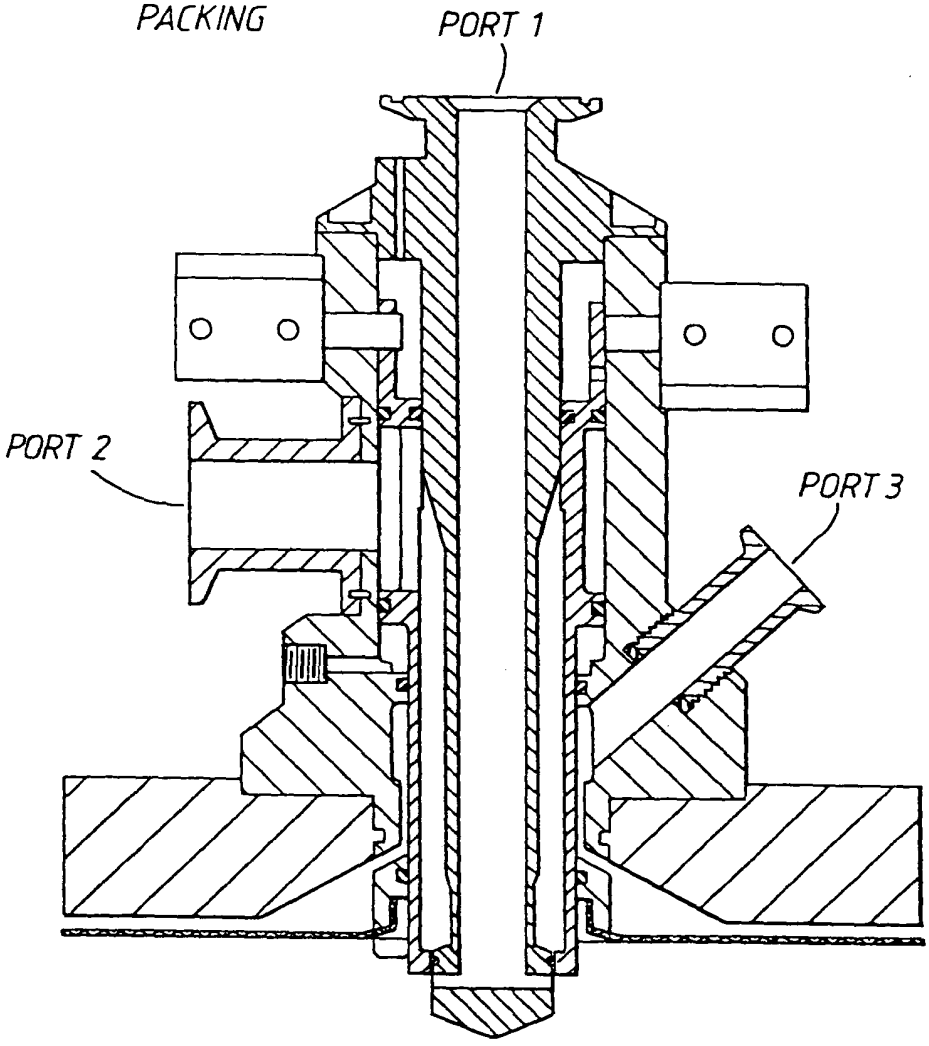

Fig. 2 (PRIOR ART)

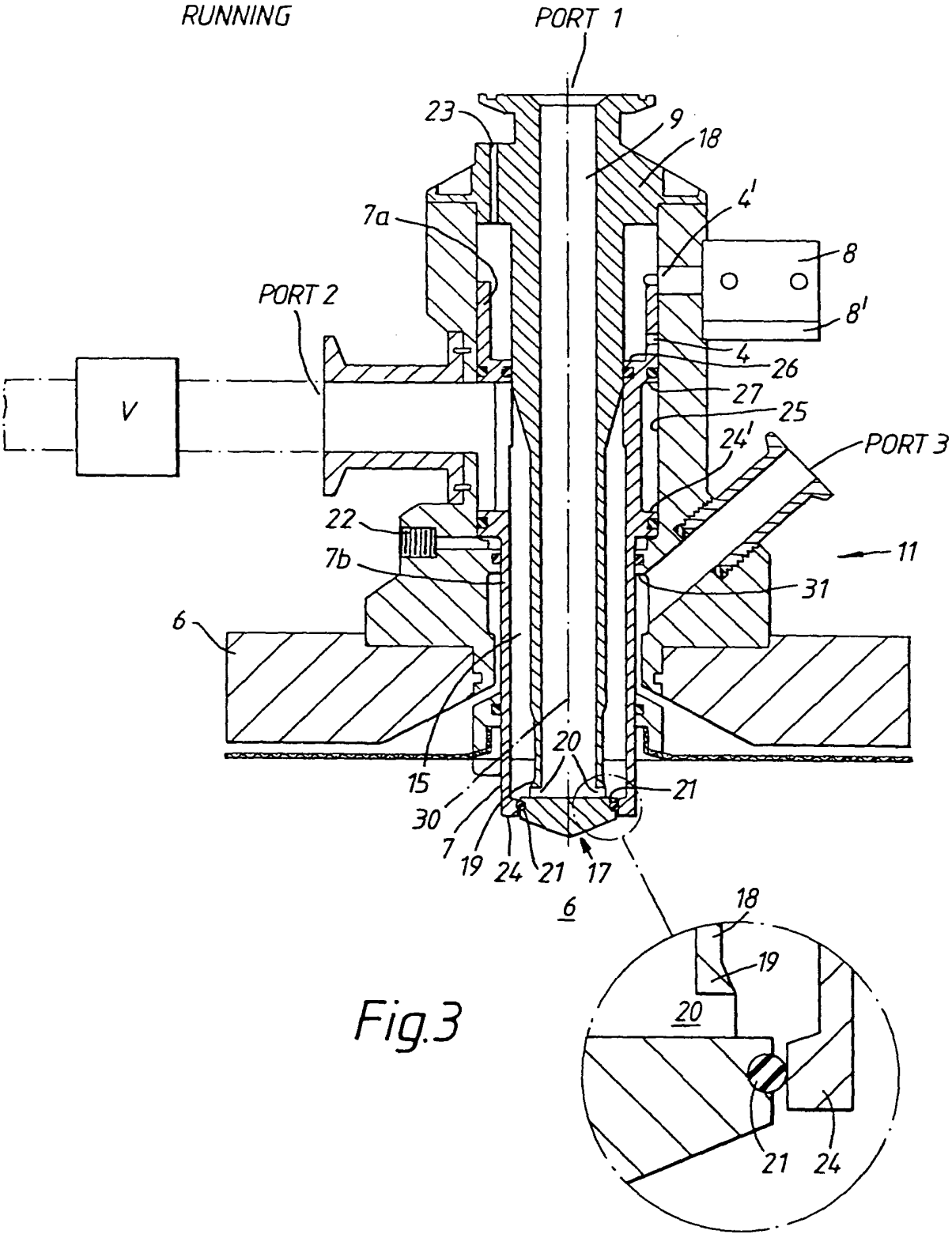
RUNNING
PORT 1
23
9
18
4'
7a
8
8'
PORT 2
4
26
27
25
V
24'
PORT 3
22
11
7b
31
6
20
15
21
30
7
19
24
21
17
6
18
19
20
21
24

Fig.3

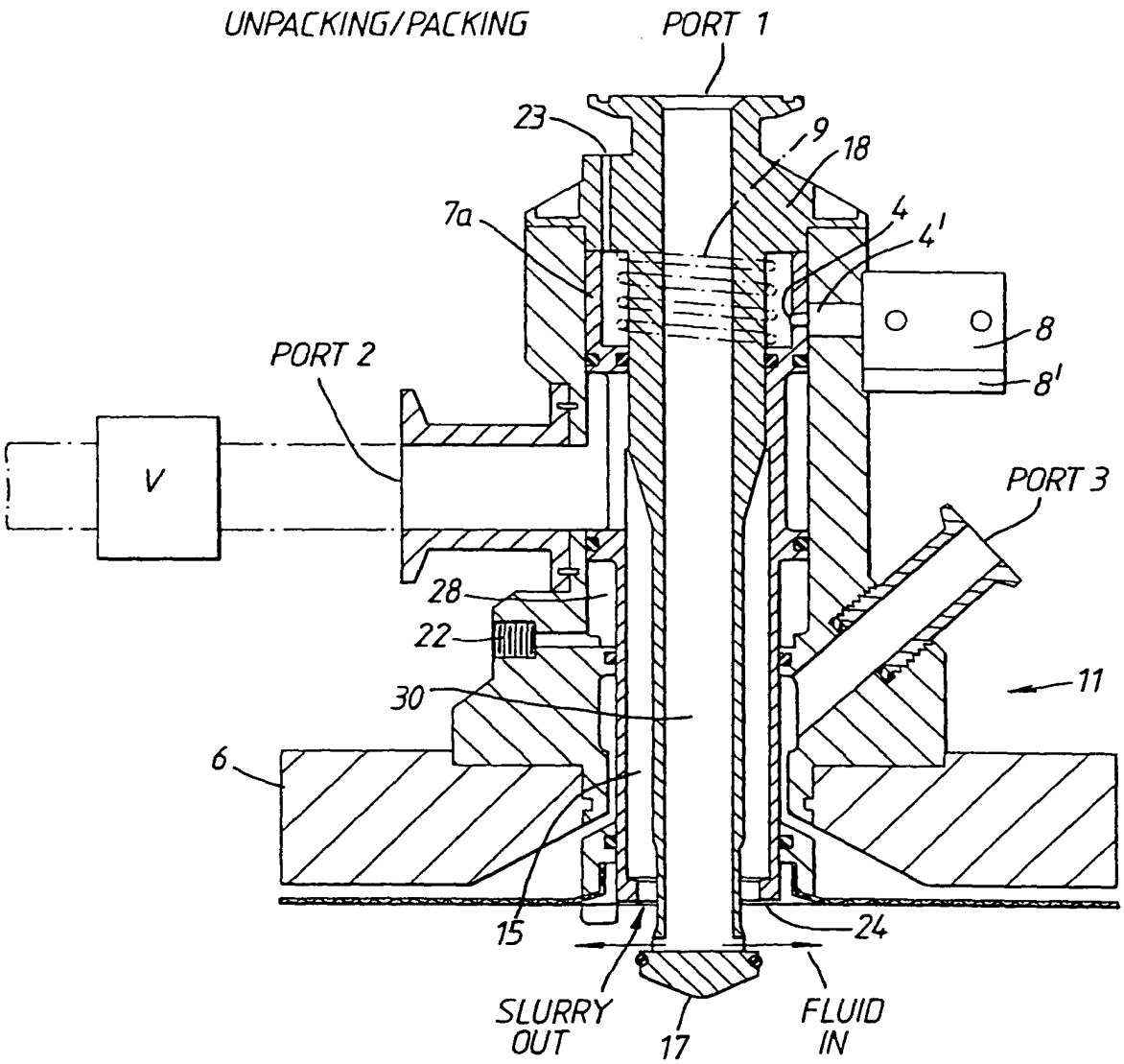
UNPACKING/PACKING
PORT 1
23
9
18
7a
4
4'
8
8'
PORT 2
V
PORT 3
28
22
30
11
6
15
24
SLURRY OUT
17
FLUID IN

Fig.4

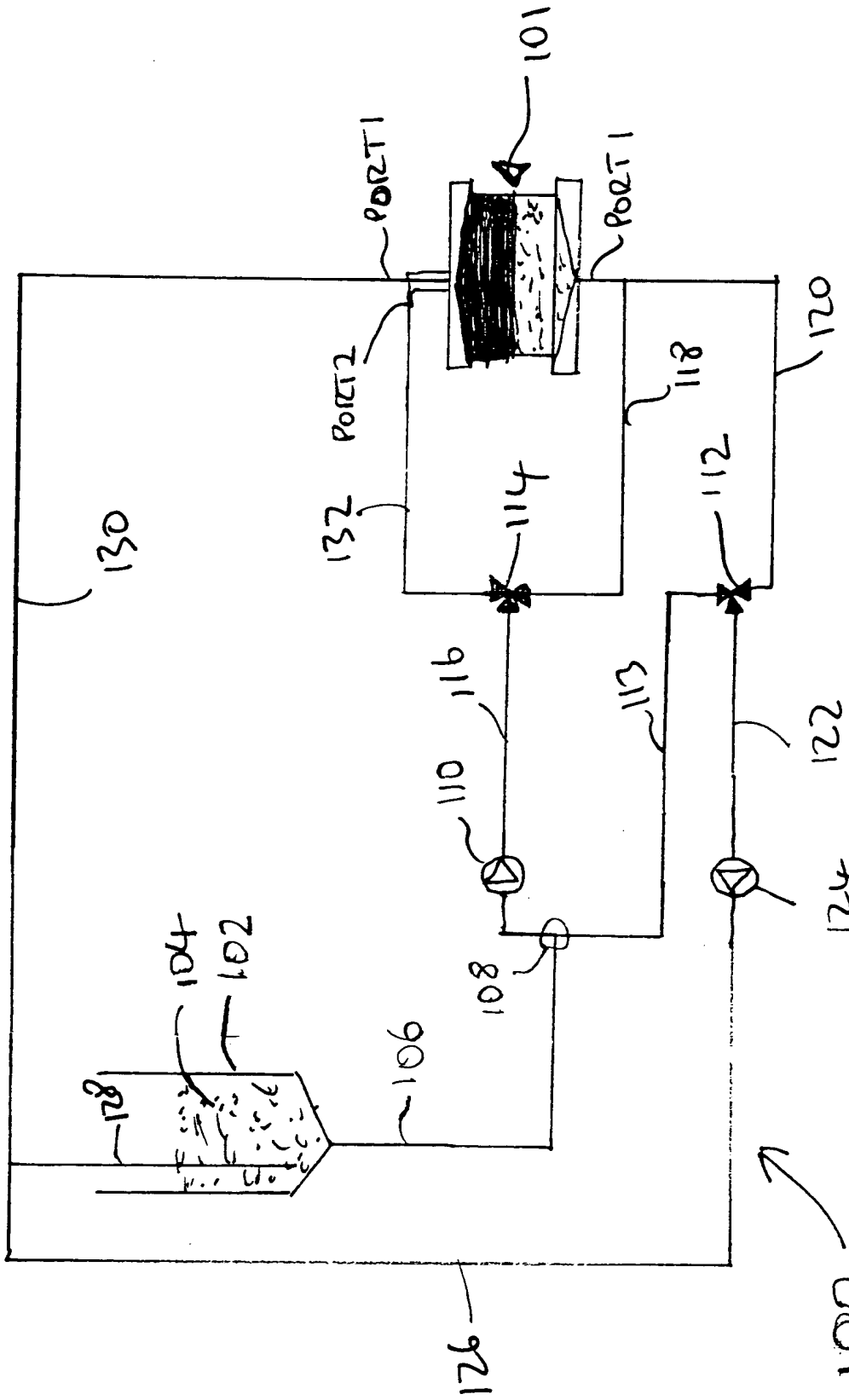
101
PORT 1
PORT 1
PORT 2
120
118
132
114
112
130
116
117
122
110
124
108
104
102
106
128
126
100

Fig 5

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Graham Watt & Co

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